The FDA Review of Efficacy of EERW Double-Blinds (FREED) of Opioids Act

The Problem

In 2020, more than 90,000 people died from a drug overdose, the highest amount ever recorded, and we can safely assume over 51% of those involved an opioid or synthetic-opioid. That's 238 people dying of a drug overdose every day. It is clear that we are facing a devastating opioid epidemic. It is also clear that the opioid market remains flooded with pills. The U.S. makes up only 4.6% of the world population, but consumes 80% of the opioids. Misuse and addiction involving prescription drugs costs the country an estimated $78.5 billion a year in lost productivity, medical costs and criminal justice costs.

The Food, Drug, and Cosmetic (FD&C) Act requires drugmakers to demonstrate their products are safe and effective by performing "adequate and well controlled studies" before they are approved. At least 2 randomized trials, with a control group and a placebo group, have generally been required to show a drug is efficacious. For the past several years FDA has deviated from this requirement, allowing use of a controversial methodology known as enriched enrollment randomized withdrawal (EERW) for approval of new opioids.

EERW trials differ from traditional double-blind, randomized, controlled studies. In an EERW trial, prior to randomization for a double-blind phase, all subjects are made physiologically dependent on the opioid in a 4- to 6-week open-label phase. Then only the patients who tolerated the opioid and found it helpful during the open-label phase are randomized to remain on the opioid or switch to a placebo.

EERW clinical trials for opioid analgesics skew findings in favor of approval. These trials are not adeaqute or well controlled for the following reasons: 1) results are not generizable to clinical practice because patients with a poor response to the open-label phase are excluded from the randomization phase; 2) Because daily use of opioids causes physiological dependence, patients switched from the opioid to placebo are likely to experience withdrawal, including increased pain sensitivity skewing results in favor of the opioid; 3) the study is not truly double-blind because the devopment of withdrawal symtoms in the placebo group are obvious to study subjects and investigators.

The FDA convenes advisory committees of scientific experts when a matter is of significant public interest, highly controversial, or in need a specific type of expertise. Unfortunatey, FDA's decision to allow EERW for opioid approvals was made after private meetings with drugmakers and without consulting its scientific advisory committees. With so many people dying every day, it seems clear that the FDA should now convene an advisory committee to review if EERW meets the FD&C Act's drug approval requirement for adequate and well controlled studies..

The Solution: The FREED of Opioids Act will ensure that scientific experts review this methodology and will ensure that opioids are only marketed for uses where they are both safe and efficacious. Specifically the bill would:

1. Require the FDA to convene a joint meeting of the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) & Drug Safety and Risk Management Advisory Committee (DSaRM), to vote on the whether EERW methodology should be used in clinical trials for opioid analgesic approvals.
2. Require the National Academy of Sciences to conduct a study on EERW and its effectiveness in proving the efficacy of opioids in treating chronic pain.